REMARKS

Claims 1-8, 12 and 15-17 were rejected, while claim 19 was objected to. Applicants respectfully request favorable reconsideration of the rejections and allowance of the present application in view of the above amendments and following remarks.

New claims 20-26 have been added to cover more preferred embodiments of Applicants' invention, as supported by the specification.

The objection to claim 19 is moot in view of its cancellation above.

Claims 1-3, 6-8, 12 and 15-17 were rejected under 35 USC 112, first paragraph, because the Examiner believes that "the specification, while being enabling for an isolated DNA encoding a protein comprising SEQ ID NO:5, 6, 21 or 25, does not reasonably provide enablement for" the isolated DNA set forth in paragraphs A-D on page 2 of the Office Action. With respect to claims 1-3, 6 and 12, the Examiner cited on pages 3-4 the absence of any "functional limitation" as a basis for the alleged lack of enablement.

The Section 112, first paragraph, rejection is traversed in view of the above claim amendments and for the following reasons. Claim 1 has been amended above to recite an isolated DNA encoding

"an isolated human estrogen receptor protein" having the recited claim features, including the added feature "wherein said DNA-binding domain targets the receptor protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to an estrogen, thereby modulating expression of said target gene." Similarly, claim 12 has been amended to recite a DNA encoding "a chimeric receptor protein" having the recited claim features, also including the above added feature. Enabling support for the above claim amendments is found in the specification, including on pages 2-3; page 5, lines 7-16; page 6, lines 11-13; pages 7-10 (homology determination); pages 11-12 (methods for preparing the receptor protein); pages 12-14 (claim 12); and both the Figures and the Examples.

The claim feature of "having in N-terminal domain" has been deleted from claim 1 as redundant, after further defining the receptor as an "estrogen receptor."

With respect to the final paragraph of ¶ No. 7 (relating to claims 7 and 8), the Examiner stated that the specification does not teach how to transfect a cell with DNA which is not in a vector. However, the technique for introducing DNA in a cell is the same for any DNA irrespective of whether the DNA is included in a vector. The specification teaches on page 11, lines 30-33, that "techniques for transforming or transfecting host cells are quite known in the art (see Sambrook et al., Molecular Cloning: A

Laboratory Manual, Cold Spring Harbor Laboratory, 1989)."

Accordingly, for the above reasons, Applicants respectfully ask that the Section 112, first paragraph, rejection be withdrawn.

Claims 1-3, 6-8 and 15-17 also were rejected under 35 USC 112, first paragraph, for an alleged lack of written description. The Examiner's basis in part was that "[c]laimed DNA encoding protein variants encompass a large genus of nuclear receptors which are alleles or variants whose function has yet to be identified from different species of animal..." This rejection is also is traversed.

Applicants' specification provides adequate written description for the unamended claims. For example, as described in the legend to Figure 4 on page 17, Figure 4 shows the expression in tissues from several different species (e.g. cell line 17 from bovine; cell 18, 19 and 21 from rat; cell line 20 from guinea pig). Additionally, once selected probes are determined, which probes can hybridize specifically to ERβ RNA in a cell, the skilled person can apply routine skill to isolate the corresponding complete cDNA without undue experimentation and with a reasonable expectation of success. More detailed information and techniques are exemplified in Examples D and E on pages 24-28. Thus, the information in Applicants' specification

makes available species homologs (also named orthologs) within the homology range specified in the claims, irrespective of the species from which the DNA is obtained.

The Eli Lilly case cited by the Examiner thus is distinguishable from the present case, at least for the above reasons and in view of the rapidly expanding capabilities in the field of the present invention.

However, to advance the prosecution, Applicants have amended claim 1 to recite an isolated DNA "encoding an isolated human estrogen receptor protein" having the recited features of the amended claim. An adequate written description of the invention, as amended, is provided in the specification, including on page 5, lines 1-20; pages 7-10, and both the Figures and the Examples. Accordingly, Applicants ask that this additional Section 112, first paragraph, rejection be withdrawn.

Claims 1-6 and 15-16 also were rejected under 35 USC 102(e) as anticipated by Cabib et al. USP (5,936,731). The Examiner has maintained that the claims encompass a isolated human chromosome because the chromosomes comprise the claimed nucleic acid molecules. Specifically, the Examiner stated that "[since] the human genome comprises all the gene sequences, the chromosomes inherently comprise the sequences claimed." The anticipation rejection is traversed for the following reasons.

Claim 1 has been amended to recite "[a]n isolated DNA encoding an isolated human estrogen receptor protein" having the recited claimed features. The amended claims do not read on a chromosome, as alleged by the Examiner, and Applicants thus ask that the rejection be withdrawn.

Furthermore, the term "isolated DNA" in the claims has the meaning commonly given to it in the molecular biology context, which is that the DNA is removed from its natural state to enable its examination in isolation. This "isolation" is from other DNA of the source genome and thus, for these additional reasons, the claims do not encompass an isolated chromosome, as asserted by the Examiner.

The rejection of claims 1-8 and 15-17 under 35 USC 103(a) as unpatentable over Cabib et al. in view of Kausch et al. also is traversed for the above reasons. Applicants thus ask that the Section 103 rejection also be withdrawn.

Finally, claim 12 was rejected under 35 USC 102(b) as anticipated by Evans et al. This rejection also is traversed for the following reasons.

Comparisons were made between the claimed invention and Evans, with the following results: In Evans, SEQ ID NO:1 and 2 is hXR 1, in which the amino acids (AA) 98-163 appear to encode the DNA-binding domain, and which is 50% homologous to the DNA-

binding domain of the present invention. SEQ ID NO:7 and 8 in Evans is hXR2, in which the DNA-binding domain appears to be AA 91-155, and which is 45% homologous to the DNA-binding domain of the present invention. SEQ ID NO:9 and 10 is mXR4, in which the DNA-binding domain appears to be AA 73-137, and which is 45% homologous to the DNA-binding domain of the present invention. SEQ ID NO:11 and 12 is mXR5, in which the DNA-binding domain appears to be AA 138-203, and which is 48% homologous to the DNA-binding domain of the present invention. SEQ ID NO:13 and 14 is dXR79, in which the DNA-binding domain appears to be AA 52-117, and which is 45% homologous to the DNA-binding domain of the present invention. Thus, the chimeric receptors of Evans are distinguishable from the present invention, and therefore Evans cannot anticipate claim 12. Accordingly, Applicants ask that the Section 102(b) rejection of claim 12 also be withdrawn.

In view of the remarks above, with the present amendments, it is believed that this application is in condition for allowance. Favorable action is thus solicited.

Should the Examiner consider that a conference would be helpful in advancing the prosecution of this application, he is invited to contact the undersigned at the number below.

In the event any fees are required with this paper, please charge our Deposit Account Number 02-2334.

Respectfully submitted,

Michael G. Sullivan
Attorney for Applicants
Registration No. 35,377

Attorney's Docket No. O/96193 US
Akzo Nobel Patent Department
1300 Piccard Drive, Suite 206
Rockville, Maryland 20850-4373
Tel: (301) 948-7400
Fax: (301) 948-9751

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1. (Twice amended) An isolated DNA encoding [a protein] an isolated human estrogen receptor protein having [an N-terminal domain] a DNA-binding domain and a ligand-binding domain, wherein the amino acid sequence of said DNA-binding domain [of said protein] exhibits at least 80% homology with the amino acid sequence shown in SEQ ID NO:3, and the amino acid sequence of said ligand-binding domain [of said protein] exhibits at least 70% homology with the amino acid sequence shown in SEQ ID NO:4, and wherein said DNA-binding domain targets the receptor protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to an estrogen, thereby modulating expression of said target gene.

2. (Twice amended) The isolated DNA according to claim 1, wherein the amino acid sequence of said DNA-binding domain [of said protein] exhibits at least 90% homology with the amino acid sequence shown in SEQ ID NO:3.

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3. (Twice amended) The isolated DNA according to claim 1, wherein the amino acid sequence of said ligand-binding domain [of said protein] exhibits at least 75% homology with the amino acid sequence shown in SEQ ID NO:4.

8. (Amended three times) The cell according to claim 7, which is a stable transfected cell line that expresses [a steroid] a human estrogen receptor protein [encoded by DNA according to claims 1 or 4].

12. (Amended four times) A DNA that encodes a chimeric receptor protein, which protein has an N-terminal domain, a DNA-binding domain, and a ligand-binding domain, wherein at least one of said domains of said chimeric protein originates from a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:21 and SEQ ID NO:25, and at least one of the other domains of said chimeric protein originates from a protein from the nuclear receptor superfamily, provided that the DNA-binding domain and the ligand-binding domain of said chimeric protein originate from different proteins, and wherein said DNA-binding domain targets the receptor

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protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to a selected steroid, thereby modulating expression of said target gene.